Amendments to the Specification

Kindly amend the paragraph starting at page 5, line 20, as follows:

(2) the process as described in the above (1), wherein the LH-RH derivative is a peptide represented by the formula 5-oxo-Pro-His-Trp-Ser-Tyr-Y-Leu-Arg-Pro-Z

wherein Y indicates a residue selected from D-Leu~~DLeu~~, ~~DAla~~D-Ala, ~~DTrp~~D-Trp, D-Ser(tBu)~~DSer(tBu)~~, D-2Nal~~D2Nal~~ and D-His(ImBzl)~~DHis(ImBzl)~~, and Z indicates NH-C_2H_5 or Gly-NH_2, respectively, or a salt thereof;

Kindly amend the paragraph starting at page 6, line 1, as follows:

(3) the process as described in the above (1), wherein the LH-RH derivative is a peptide represented by the formula

5-oxo-Pro-His-Trp-Ser-Tyr- D-Leu ~~DLeu~~-Leu-Arg-Pro-NH-C_2H_5

or its acetate;

Kindly amend the paragraph starting at page 8, line 13, as follows:

(15) the process as described in the above (13) or (14), wherein the LH-RH derivative protected with protective group(s) is represented by the formula

5-oxo-Pro-His-Trp-Ser-Tyr-Y-Leu-Arg(X)-Pro-Z

wherein X indicates a protective group, Y indicates a residue selected from D-Leu~~DLeu~~, D-Ala~~DAla~~, D-Trp~~DTrp~~, D-Ser(tBu)~~DSer(tBu)~~, D-2Nal ~~D2Nal~~ and D-His(ImBzl)~~DHis(ImBzl)~~ and Z indicates NH-C_2H_5 or Gly-NH_2, respectively;

Kindly amend the paragraph starting at page 9, line 9, as follows:

Examples of the LH-RH agonist include peptide LH-RH derivatives possessing LH-RH agonistic activity and salts thereof and there are, for example, peptide LH-RH derivatives possessing LH-RH agonistic activity and salts thereof that are effective against hormone-dependent diseases, particularly sex hormone-dependent cancers (for example, prostatic cancer, uterine cancer, breast cancer, pituitary tumor and the like), prostatic hypertrophy, endometriosis,

uterine myoma, precocious puberty, dysmenorrhea, amenorrhea, premenstrual syndrome and polysystic ovary syndrome, as well as for contraception (or against infertility if the post-withdrawal rebound effect is exploited). In addition, they include, for example, LH-RH derivatives and salts thereof, which are effective against benign or malignant tumors that are LH-RH-sensitive though being sex hormone-independent~~, etc~~.

Kindly amend the paragraph starting at page 10, line 12, as follows:

Examples of such a salt, in the case where said LH-RH derivative has an acidic group such as carboxyl group or the like, include a salt with an inorganic base (also, designated as an inorganic free base) (for example, an alkali metal such as sodium, potassium~~, etc.~~, an alkaline earth metal such as calcium, magnesium~~, etc.~~, or the like), a salt with an organic base (also, designated as an organic free base) (for example, an organic amine such as triethylamine~~, etc.~~, a basic amino acid such as arginine~~, etc.~~) or the like. In addition, said LH-RH derivative may form a metal complex compound (for example, a copper complex, a zinc complex or the like).

Kindly amend the paragraph starting at page 11, line 12, as follows:

In the above-mentioned formula (I), the D-amino acid residue indicated by R3 is exemplified by an a-D-amino acid having up to 11 carbon atoms (for example, D-Leu, Ile, Nle, Val, Nval, Abu, Phe, Phg, Ser, Thr, Met, Ala or Trp) or the like, each of which may have 1 to 3 adequate substituents (for example, a C_{1-4} alkyl group such as methyl, t-butyl~~, etc.~~, a C_{1-4} alkoxyl group such as t-butoxy~~, etc.~~, a C_{1-4} alkoxycarbonyl group such as t-butoxycarbonyl~~, etc.~~, a C_{6-10} aryl group such as 2-naphthyl~~, etc.~~, an indolyl group or an imidazolyl group, which may be substituted with C_{1-4} alkyl, C_{6-10} aryl or C_{6-10} aryl-C_{1-4} alkyl, respectively, such as indolyl-3-yl, 2-methylindolyl, benzylimidazol-2-yl~~, etc.~~, or the like). Examples of the substituent of an alkyl group that may be substituted, which is indicated by R_6, include hydroxyl or amino. The alkyl group of an alkyl group that may be substituted with amino group or hydroxyl group is exemplified by a C_{1-4} alkyl group and a C_{1-3} alkyl group is especially preferred. Examples of a C_{1-4} alkyl group include methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl or tert-butyl. The number of substituents is, for example, 1 to 3, where 1 to 2 substituents are preferable and one substituent is particularly preferable.

Kindly amend the paragraph starting at page 12, line 10, as follows:

More preferably, examples of the peptide LH-RH derivative possessing LH-RH agonistic activity include a physiologically active peptide represented by the formula (II)

5-oxo-Pro-His-Trp-Ser-Tyr-Y-Leu-Arg-Pro-Z

wherein Y indicates a residue selected from D-Leu~~DLeu~~, D-Ala~~DAla~~, D-Trp~~DTrp~~, D-Ser(tBu)~~DSer(tBu)~~, D-2Nal ~~D2Nal~~ and D-His(ImBzl)~~DHis(ImBzl)~~, and Z indicates NH-C_2H_5 or Gly-NH_2, respectively, and a salt thereof~~, etc~~. Particularly preferable is such a peptide in which Y is D-Leu~~Dleu~~ and Z is NH-C_2H_5 (namely, the peptide represented by 5-oxo-Pro-His-Trp-Ser-Tyr-D-Leu~~DLeu~~-Leu-Arg-Pro-NH-C_2H_5: leuprorelin). As for a salt of the peptide represented by 5-oxo-Pro-His-Trp-Ser-Tyr-D-Leu~~DLeu~~-Leu-Arg-Pro-NH-C_2H_5, its acetate (leuprorelin acetate) is particularly preferred among those exemplified as mentioned above.

Kindly amend the paragraph starting at page 12, line 25, as follows:

The abbreviations used herein for denoting amino acids, peptides, protective groups, ~~etc.,~~ in the polypeptides are those according to IUPAC-IUB Commission on Biochemical Nomenclature or conventional codes in this art field, and, also, in the case where an optical isomer may exist with regard to an amino acid, it shall be indicated by the L form, unless otherwise specified.

Kindly amend three consecutive abbreviations beginning at page 14, line 3, as follows:

D-2Nal~~D2Nal~~	: D-3-(2-Naphthyl)alanine residue
D-Ser(tBu) ~~DSer(tBu)~~	: O-tert-Butyl-D-serine
D-His(ImBzl)~~DHis(ImBzl)~~	: N^{im}-Benzyl-D-histidine

Kindly amend the paragraph starting at page 17, line 11, as follows:

The methacrylic synthetic adsorption resin means a synthetic adsorption resin of a polymer whose substrate is a methacrylic acid ester, and racemic isomers~~, etc.~~ of the LH-RH derivative can be unexpectedly and effectively removed by subjecting a solution containing the LH-RH derivative to a step for treatment with said resin (particularly by the use of an aromatic,

synthetic adsorption resin as described hereinafter in combination) to prepare (purify) the LH-RH derivative.

Kindly amend the paragraph starting at page 17, line 20, as follows:

In addition, racemic isomers~~, etc.~~ of the LH-RH derivative can be effectively removed so that a step for treatment with columns in multi stages, which has been heretofore carried out, can be shortened.

Kindly amend the paragraph starting at page 18, line 4, as follows:

Specific examples of the methacrylic synthetic adsorption resin column include HP 2MG (manufactured by Mitsubishi Chemical Corporation), XAD-7 and XAD-8 (manufactured by Organo Company) and the like (preferably, HP 2MG (manufactured by Mitsubishi Chemical Corporation~~), etc.~~), but any one may be used as far as it achieves the object to effectively remove racemic isomers, etc. of the LH-RH derivative.

Kindly amend the paragraph starting at page 18, line 19, as follows:

Particularly, in the case where the above-mentioned leuprorelin (leuprorelin acetate) is prepared (purified) with the methacrylic synthetic adsorption resin (preferably, HP 2MG (manufactured by Mitsubishi Chemical Corporation~~), etc.~~), there can be very effectively removed a racemic isomer at His adjacent to 5-oxo-Pro in leuprorelin (leuprorelin acetate) (hereinafter, abbreviated as D-His^2 form), a racemic isomer at Trp adjacent to His (hereinafter, abbreviated as D-Trp^3 form) and other highly polar related substances.

Kindly amend the paragraph starting at page 19, line 14, as follows:

The aromatic synthetic adsorption resin (preferably, a styrene-divinylbenzene synthetic adsorption resin) means a synthetic adsorption resin of a porous polymer, which is prepared by copolymerization of styrene and divinylbenzene, where racemic isomers~~, etc.~~ of the LH-RH derivative can be unexpectedly and effectively removed by subjecting a solution containing the LH-RH derivative to a step for treatment with said resin (particularly by the use of the methacrylic synthetic adsorption resin described above in combination) to prepare (purify) the

LH-RH derivative. Specific examples of the aromatic synthetic adsorption resin include HP 20 and HP 21 (manufactured by Mitsubishi Chemical Corporation), HP 20SS and SP 20SS (manufactured by Mitsubishi Chemical Corporation), XAD-2 and XAD-4 (manufactured by Organo Company) and the like (preferably, HP 20SS (manufactured by Mitsubishi Chemical Corporation) and the like), but any one may be used as far as it achieves the object to effectively remove racemic isomers, etc. of the LH-RH derivative.

Kindly amend the paragraph starting at page 21, line 3, as follows:

In order to achieve the above-mentioned object to "effectively remove racemic isomers~~, etc.~~ of an LH-RH derivative", it is preferable to employ a step for treatment with the methacrylic synthetic adsorption resin and a step for treatment with the aromatic synthetic adsorption resin in combination. In this case, the order of the step for treatment with the methacrylic synthetic adsorption resin and the step for treatment with the aromatic synthetic adsorption resin is not specified particularly in the process for preparing (purifying) the LH-RH derivative, but it is preferable to prepare (purify) the LH-RH derivative by subjecting it to the step for treatment with the methacrylic synthetic adsorption resin and then to the step for treatment with an aromatic, synthetic adsorption resin.

Kindly amend the paragraph starting at page 33, line 18, as follows:

The hydroxyl group of serine can be protected, for example, by esterification or etherification. Examples of the group suitable for this esterification include a lower (C_{1-6}) alkanoyl group such as acetyl group~~, etc.~~, an aroyl group such as benzoyl group~~, etc.~~, a group, which can be derived from carbonic acid, such as benzyloxycarbonyl group, ethoxycarbonyl group~~, etc.~~, and the like. In addition, examples of a group suitable for the etherification include benzyl group, tetrahydropyranyl group, t-butyl group and the like.

Kindly amend the paragraph starting at page 34, line 16, as follows:

Specifically, examples of the LH-RH derivative that is protected with protective groups include a peptide represented by the formula (III)

5-oxo-Pro-His-Trp-Ser-Tyr-Y-Leu-Arg(X)-Pro-Z

wherein X indicates a protective group, Y indicates a residue selected from D-Leu~~DLeu~~, D-Ala~~DAla~~, D-Trp~~DTrp~~, D-Ser(tBu)~~DSer(tBu)~~, D-2Nal ~~D2Nal~~ and D-His(ImBzl)~~DHis(ImBzl)~~ and Z indicates NH-C_2H_5 or Gly-NH_2, respectively, or a salt thereof.